REMARKS

Claims 1-4, 6-10, 18-24 and 35 were in the case prior to this amendment. Claim 1 has been amended above. Claims 1-4, 6-10, 18-24 and 35 remain in the case.

The Office Action

In the Office Action, the Examiner renewed the claim rejections made under 35 USC § 103(a). Specifically, claims 1-4, 8-10, 18-24 and 35 were rejected as being non-patentable over U.S. Published Patent Application No. 2003/0054046 (now U.S. Patent No. 6,939,568) to Burrell et al. ("**Burrell**"). Claims 6-7 were rejected as being unpatentable over **Burrell** in view of Schonfeld et al. (U.S. Patent No. 4,646,730) ("**Schonfeld**").

In the Office Action, the Examiner also made a new rejection of claims 1-4, 8-10, 18-24 and 35 under 35 USC § 103(a) as being non-patentable over U.S. Published Patent Application No 2002/0051823 by Yan et al. ("**Yan**") in view of U.S. Published Patent Application No. 2002/0122832 by Hanke et al. ("**Hanke**") and U.S. Patent No. 4,983,385 to Hasegawa et al. ("**Hasegawa**").

In addition, the Examiner raised nonstatutory Double Patenting rejections of claims 1-4, 6-10, 18-24 and 35 as being unpatentable over claims 1-14 of U.S. Patent No. 7,135,195 in view of **Burrell**. In addition, claims 1-4, 6-10, 18-24 and 35 were provisionally rejected under obviousness-type double patenting as being unpatentable over claims 1-10 of copending U.S. Patent Application No. 11/813,408.

When allowable material is identified in the instant application, a Terminal Disclaimer in the proper form to overcome the rejection based on **Burrell** will be filed. Applicants respectfully submit that the rejection based on copending U.S. Patent Application No. 11/813,408 is not yet ripe for action. Before a Terminal Disclaimer is necessary, allowable material will have to be identified in both pending applications. It is

possible that at that time the scope of allowable claims of U.S. Patent Application No. 11/813,408 will no longer overlap with the instant application. When it becomes clear that allowable claims actually overlap, a Terminal Disclaimer in the proper form to overcome the rejection based on U.S. Patent Application No. 11/813,408 will be filed.

Claim rejections under 35 USC § 103

The Examiner renewed rejected claims 1-4, 8-10, 18-24 and 35 as being unpatentable over **Burrell**. Applicants respectfully repeat their traverse of this finding. As stated in a previous paper, Applicants greatly appreciate the careful manner in which the Examiner has laid out the Graham factors. In response to argument that the Examiner had not clearly determined the level of ordinary skill in the art, the Examiner pointed out that the MPEP "indicates that an obviousness rejection can include implicitly an indication of the level of ordinary skill in the art." Applicants assume that the Examiner is referring to 2141.03 >II which discusses the Chore-Time case. Applicants respectfully point out that that case is not on point here. That case involved not patent prosecution before the Office but rather whether or not the trial court' failure to make an explicit determination of the level of ordinary skill was reversible error. This point is clarified by the Federal Circuit in *Ruiz v. A.B. Chance Co. (234 F.3d 654 (Fed. Cir. 2000)* where the court held that case law clearly establishes that whether failure to explicitly determine the level of skill is error turns on whether failure to make the determination influences the ultimate conclusion under section 103. Where the failure to explicitly make the determination does influence the conclusion under section 103, that failure is reversible error.

It is Applicants' respectful contention that one of ordinary skill in the art would indeed be aware of the range of ingredients and results cited by the Examiner. The person of ordinary skill in the art would also be aware of the long history of silver use and would be well aware of the extremely wide variations in results and effectiveness of various silver compositions. Therefore, one of ordinary skill in the art would realize that

a great many combinations and compositions are not effective. This goes towards predictability or reasonable expectation of success. Certainly, one of ordinary skill in the art would be motivated to produce a successful product, but one of ordinary skill in the art would not waste his or her time in making numerous combinations without a reasonable expectation of success. Were the level of ordinary skill in the art explicitly defined, as is required by the Supreme Court, it might be possible to demonstrate how one of ordinary skill would avoid the tangle of the prior art to arrive at a reasonable expectation of success. However, such a definition has not been provided. Without the Applicants' own results one of ordinary skill in the art would NOT have a reasonable expectation of success. Relying on Applicants' results is impermissible hindsight.

The Examiner tried to explore Applicants' concerns about the level of skill in the art by analyzing (pages 8 and 9 of the Office Action) how Applicants' relatively restricted range of silver fits into the broader range of the prior art. The Examiner concluded that the examples provided in **Burrell** "would enable one of ordinary skill in the art to formulate silver hydrogels with the lower limits as these amounts were found to be effective." Applicants strongly disagree with this statement because the Examiner is certainly misreading **Burrell**. First, the Examiner claims that example 1 of **Burrell** as providing evidence for the effectiveness of 66 ppm silver. Applicants' invention consists solely of silver metal particles having surface entirely coated with silver oxide. The specification goes to considerable lengths to indicate that the material is particulate and not ionic. Example 1 of **Burrell** describes a blue colored silver coating on a polyethylene substrate. The coating has a base layer 900nm thick with a top layer 100nm thick (it is not clear how the base layer differs from the top layer but presumably the top layer is at least partially silver oxide). According to the reference SEM shows that the coating is composed of columnar nanocrystals having an average grain size of 10 nm. This coating releases silver into water with an equilibrium concentration of 66 mg/l (66 ppm) silver which is "50 to 100 times higher than is expected from bulk silver metal (solubility

≤ 1mg/l).” Applicants respectfully point out that this example has absolutely nothing to do with the currently claimed invention of silver nanoparticles in water. Rather **Burrell** is demonstrating that certain coatings of silver on plastic release 66 ppm of dissolved silver (that is ionic silver). It is not at all surprising that such a concentration of ionic silver shows an inhibitory effect on bacteria. Part of the **Burrell** invention is the discovery that certain metals formed with atomic disorder release “ions, clusters, atoms or molecules . . . at a concentration sufficient to provide a localized antimicrobial and anti-inflammatory effect.” (column 6 at lines 48-51). Similarly, the Examiner argues that example 4 of **Burrell** teaches a level of 10 ppm silver. Again, this example fails to teach anything about particulate silver having a silver concentration of 10 ppm. Rather the examples shows that silver (again, apparently ionic silver) can be eluted from a commercial dressing (Acticoat Burn Wound Dressing). The eluted silver was determined to have a concentration of 20 ppm and was diluted to 10 ppm silver in the bacteriological test where that concentration of silver produced a 4.3 log reduction in viable bacteria within two hours. In summary neither of the examples cited by the Examiner demonstrates the effectiveness of 66 ppm or 10 ppm silver nanoparticles. Rather the examples show the effectiveness of 66 ppm and 10 ppm soluble silver that can be eluted from properly prepared silver coated surfaces. One of ordinary skill in the art would know that results using soluble silver provide little if any useful information concerning nanoparticulate silver because these are two different materials. The fact remains that the examples in **Burrell** where effectiveness of particulate silver is demonstrated use compositions containing at least 0.1% silver powder (1000 ppm silver) which is orders of magnitude higher than the silver in the present invention. It remains that **Burrell** would cause one of skill in the art to expect silver particles at 50 ppm total silver concentration to be ineffective.

The experiments presented in the instant application show that silver particles of a particular composition and size range are clearly effective at extremely low

concentrations. However, **Burrell** does not teach silver particles having the size and composition of the instant invention. Nor is there anything in **Burrell** to suggest to one of ordinary skill in the art that making silver particles with the composition and size of the instant invention would provide these unusual properties. Applicants respectfully contend that the differences between their invention and the prior art include the use of silver particles having a certain defined range and having a structure wherein the core of the particle is metallic silver and the entire surface of the particle is coated with silver oxide. Applicants respectfully contend that nothing in the prior art would lead one of ordinary skill in the art to make such a composition.

The new rejection of claims 1-4, 8-10, 18-24 and 35 under 35 USC § 103(a) as being non-patentable over U.S. Published Patent Application No 2002/0051823 by Yan et al. ("**Yan**") in view of U.S. Published Patent Application No. 2002/0122832 by Hanke et al. ("**Hanke**") and U.S. Patent No. 4,983,385 to Hasegawa et al. ("**Hasegawa**") fails for similar reasons. Whereas the present invention utilizes a suspension of nanoparticles having a silver core and a surface coated by silver oxide suspended in water, the material of **Yan** consists of NAGs which are particles of ground up pith on which has been deposited silver particles prior to grinding. Thus, one of ordinary skill would recognize that whereas the present invention comprises nanoparticles which are free to diffuse through the matrix of a gel, the **Yan** particles are bound to larger granules of plant material and are not free to diffuse. Furthermore, the data provided in the reference suggest that the NAGs are not effective at low silver concentrations. Paragraph 0063 indicates that the NAGs are 2-8% by weight silver. The disinfectant tests of Example 2 were conducted using a solution that contained 1 g of NAG per 100 ml. Because the 1NAG was 2-8% by weight silver, the 100 ml of solution contained between 20 and 100 mg of silver as mentioned by the Examiner. However, 20-100 mg per 100 ml represents 200-1000 ppm silver which is much higher than the present invention. Thus, not only is the physical state (particles bound to larger granules of

organic matter) of the silver particles in **Yan** different from those of the instant invention but also the material is used at a higher silver concentration, thereby implying to one of skill in the art that the NAG particles are less active.

The Examiners states that **Hanke** cures any silver concentration problem. However, a careful reading of that reference does not solve the silver concentration problem. **Hanke** teaches an invention where silver is deposited on a surface. In example 1 the surface is polypropylene with a 10 nm silver coating. This material was shredded into granules which were then remolded into an item having approximately 2000 ppm silver. In example 2 the deposition surface was that of liquid silicone oil. This produces an oil containing silver nanoparticles. The oil was either coated on other items or molded into plastics, etc. When molded into the topsheet of a diaper, the sheet contained 1000 ppm silver. When silicone oil containing 1% by weight silver was mixed into a lotion (example 3) a lotion with 50 ppm silver was tested the "vitality of the germs was greatly reduced and proliferation considerably limited." However lotion with 250 ppm silver completely eliminated the germ. Again, these tests show that the silver particles of **Hanke** are less effective than those of the present invention. Further, one of ordinary skill in the art would understand that particles formed from a coating evaporated onto a surface (solid plastic or oil) would not have a silver oxide surface because the metal deposited against the surface would be protected from oxidation.

Further, one of ordinary skill in the art would find the claims of this reference confusing at best. Paragraph [0013] clearly states that the silver nanoparticles provide a silver concentration 1 μmol/l to 1 nmol per liter (i.e. 108×10^{-6} g to 108×10^{-9} g/l or between about 0.1 and 0.01 ppm silver). Paragraph [0014] states that the "organic matrix in contact with the human of animal skin comprises said silver nanoparticles in an amount from 1 to 2000 ppm, preferably from 5 to 1000 ppm and more preferably from 10 to 250 ppm." One of ordinary skill in the art would realize that the silver concentration expressed in molar fashion seems to conflict with that expressed in parts per million.

However, paragraph [0014] (as well as claim 3 which appears derived from this paragraph) does not state parts per million of silver. Rather, it states parts per million of particles. Finally, all the compositions of **Hanke** are based on hydrophobic viscous liquids rather than hydrogels. Nor are the problems of silver concentration and hydrogels corrected by **Hasegawa**. That reference teaches that it is possible to produce an ointment base that clings to wet surfaces by combining a hydrogel with a methacrylate copolymer (which is not water soluble) with a solvent that dissolves the copolymer while being incompatible with water. The reference teaches that certain pharmaceutical agents are active in this ointment base. However, silver is not mentioned as being one of the possible agents. Thus **Yan** does not teach free silver particles nor does it teach the same effective silver concentrations. **Hanke** teaches free silver particles (albeit not with an oxide surface) in a hydrophobic composition (no hydrogel). **Hanke** does not demonstrate effectiveness at the same low silver concentrations as the present invention. **Hasegawa** provides a non-silver ointment that contains a hydrogel component but is clearly not a hydrogel. Applicants respectfully contend that no combination of the cited art would provide the instant invention or cause one of skill in the art to have a reasonable expectation of success in using free silver particles having the characteristics of Applicants' particles in a hydrogel. Applicants respectfully request the withdrawal of the rejections based on **Burrell**, **Yan**, **Hanke** or **Hasegawa**.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested. If for any reason the Examiner still finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (310) 229-9928 to discuss the steps necessary for placing the application in condition for allowance. You are hereby

authorized to charge any fees due and refund any surplus fees to our Deposit Account No. 22-0261. Please reference matter number 80663.251821.

Respectfully submitted,

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